MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: July 20, 2022
Effective Date: August 23, 2022

Comprehensive Nephrology Gene Panel, Varies

Test ID: NEPHP

Useful for:

- Providing a genetic evaluation for patients with a personal or family history suggestive of hereditary kidney disease
- Establishing a diagnosis for a variety of hereditary kidney conditions including focal segmental glomerulosclerosis, nephritic/nephrotic syndrome, Alport syndrome, cystic kidney diseases (including polycystic kidney disease), nephronophthisis, tubulointerstitial disease, congenital anomalies of kidney and urinary tract, nephrocalcinosis, nephrolithiasis (kidney stones), renal electrolyte imbalances (including Bartter syndrome), C3 glomerulopathy, and complement-mediated thrombotic microangiopathy (also known as atypical hemolytic uremic syndrome)

Genetics Information:

This test utilizes next-generation sequencing to detect single nucleotide, deletion-insertion, and copy number variants in 302 genes associated with hereditary kidney disease: *ABCC6, ACE, ACTN4, ADAMTS13, ADCY10, AGT, AGTR1, AGXT, AHI1, ALG1, ALG8, ALG9, ALMS1, ALPL, ANKS6, ANLN, ANOS1, APOA1, APOE, APOL1* [Chr22(GRCh37]:g.36661895-36661916 and g.36662023-36662062 only), *APRT, AP2S1, AQP2, ARHGAP24, ARHGDIA, ARL13B, ARL6, ATP6V0A4, ATP6V1B1, ATP7B, AVP, AVPR2, B9D1, B9D2, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BICC1, BSND, C2, C2CD3, C3, C5* [Chr9(GRCh37):g.123759950-123759973 only], *C8A, C8orf37, CA2, CACNA1D, CACNA1H, CASR, CC2D2A, CD151, CD2AP, CD46* (*MCP*), *CEP104, CEP120, CEP164, CEP290, CEP41, CEP83, CFB, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5, CFI, CHD7, CLCN5, CLCNKA, CLCNKB, CLDN16, CLDN19, CNNM2, COL4A1, COL4A3, COL4A4, COL4A5, COL4A6, COQ2, COQ6, COQ8B, CPLANE1, CRB2, CREBBP, CSPP1, CTNS, CUBN, CUL3, CYP11B1, CYP11B2, CYP24A1, CYP27B1, CYP2R1, DCDC2, DDX59, DGKE, DHCR7, DMP1, DNAJB11, DYNC2H1, DZIP1L, EGF, EMP2, ENPP1, EYA1, FAH, FAM20A, FAN1, FAT1, FGA, FGF20, FGF23, FGFR1, FGFR2, FN1, FOXI1, FOXP1, FRAS1, FREM1, FREM2, FXYD2, GALNT3, GANAB, GATA3, GLA, GLI3, GLIS2, GNA11, GPC3, GREB1L, GRHPR, GRIP1, GSN, HNF1B, HNF4A, HOGA1, HPRT1, HPSE2, HSD11B2, IFT122, IFT140, IFT172, IFT27, IFT43, IFT80, IFT81, INF2, INPP5E, INVS, IQCB1, ITGA3, ITGA8, ITGB4, JAG1, KANK2, KCNA1, KCNJ1, KCNJ10, KCNJ5, KIAA0556* (*KATNIP*), *KIAA0586, KIAA0753, KIF12, KIF14, KIF7, KL, KLHL3, LAMA5, LAMB2, LMNA, LMX1B, LRIG2, LRP2, LRP5, LYZ, LZTFL1, MAGED2, MAGI2, MAPKBP1, MEFV, MKKS, MKS1, MMACHC, MOCOS, MYH9, MYO1E, NEK1, NEK8, NLRP3, NOTCH2, NPHP1, NPHP3, NPHP4, NPHS1, NPHS2, NR3C2, NUP107, NUP133, NUP160, NUP205, NUP85, NUP93, OCRL, OFD1, PAX2, PBX1, PCBD1, PDE6D, PDSS2, PHEX, PKD1, PKD2, PKHD1, PLCE1, PLCG2, PLG, PMM2, PODXL, PRKCSH, PRPS1, PTPRO, REN, ROBO2, RPGRIP1L, SALL1, SALL4, SARS2, SCARB2, SCLT1, SCNN1A, SCNN1B, SCNN1G, SDCCAG8, SEC61A1, SEC63, SGPL1, SIX1, SLC12A1, SLC12A3, SLC17A5, SLC22A12, SLC26A1, SLC2A2, SLC2A9, SLC34A1, SLC34A3, SLC3A1, SLC4A1, SLC4A4, N27,SLC5A1, SLC5A2, SLC6A19, SLC7A7, SLC7A9, SLC9A3R1, SLIT2, SMARCAL1, TBC1D8B, TBX18, TCTN1, TCTN2, TCTN3, THBD, TMEM107, TMEM138, TMEM216, TMEM231, TMEM237, TMEM67, TRAF3IP1, TRIM32, TRPC6, TRPM6, TSC1, TSC2, TTC21B, TTC8, TTR, UMOD, VDR, VHL, VIPAS39, VPS33B, WDR19, WDR35, WDR72, WDR73, WNK1, WNK4, WNT4, WT1, XDH, XPNPEP3, ZMPSTE24, ZNF423.*

Identification of a pathogenic variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for a variety of hereditary kidney diseases.

Methods:

Sequence Capture and Amplicon-Based Next Generation Sequencing (NGS)

Reference Values:

An interpretive report will be provided.

Ordering Guidance:

- Targeted testing for familial variants (also called site-specific or known mutations testing) is available for the genes on this panel. See FMTT / Familial Mutation, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.
- Customization of this panel and single gene analysis for any gene present on this panel are available. For more information, see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Specimen Requirements:

Patient Preparation:	A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.
Specimen Type:	Whole blood
Preferred:	Lavender top (EDTA) or yellow top (ACD)
Acceptable:	Any anticoagulant
Specimen Volume:	3 mL
Collection Instructions:	1. Invert several times to mix blood. 2. Send whole blood specimen in original tube. **Do not** aliquot.
Specimen Stability Information:	Ambient (preferred)/Refrigerated
Minimum Volume:	1 mL

Note:

Specimen preferred to arrive within 96 hours of collection**.**

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Cautions:

Clinical Correlations:

- Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.
- To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

- Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.
- This gene panel does **not** include assessment or interpretation of the common *APOE* alleles e2, e3, or e4.
- There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.
- This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

- This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.
- This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.
- Genes may be added or removed based on updated clinical relevance. For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.
- If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

- At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:

- Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(10) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.
- Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools are interpreted with caution and professional clinical judgement.
- Rarely, incidental findings or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

CPT Code:
81401 x2
81404 x12
81405 x8
81406 x22
81407 x13
81408 x5
81479

Day(s) Performed: Varies

Report Available: 28 to 42 days

Note:
The following referral test code(s) will become obsolete.

Test Name	Test ID	Referral Lab Code	Referral Lab
Acrocallosal, Fetal Hydrolethalus, and Joubert Syndromes via the KIF7 Gene	ZW194	11031	Prevention Genetics Lab
Apparent Mineralocorticoid Excess via the HSD11B2 Gene	ZW194	9969	Prevention Genetics Lab
AQP2 (Nephrogenic Diabetes Insipidus) DNA Sequencing Test	ZW127	852	Athena Diagnostics
Autosomal Dominant Pseudohypoaldosteronism Type 1 via the NR3C2 Gene	ZW194	11527	Prevention Genetics Lab
Gitelman Syndrome via the SLC12A3 Gene	ZW194	4503	Prevention Genetics Lab
Hypercalcemic and Hypocalcemic Disorders via the GNA11 Gene	ZW194	11359	Prevention Genetics Lab
Hypophosphatasia via ALPL Gene Sequencing with CNV Detection	ZW194	7573	Prevention Genetics Lab
Hypophosphatasia, infantile, childhood & adult types	ZW193	1565	Connective Tissue Gene Tests Lab
Infantile Hypercalcemia	ZW199	MML1197	Nemours Children's Health-Molecular
JAG1 Gene Analysis in Alagille Syndrome Sequencing and Exon Array Dx of the entire gene NOW	ZW168	1004	GeneDx, Inc.
Lesch-Nyhan Syndrome, HPRT-Related Hyperuricemia and Gout via the HPRT1 Gene	ZW194	7129	Prevention Genetics Lab
Liddle Syndrome and Autosomal Recessive Pseudohypoaldosteronism Type 1 via the SCNN1B Gene	ZW194	11649	Prevention Genetics Lab
Nail-Patella Syndrome via the LMX1B Gene	ZW194	8581	Prevention Genetics Lab
Simpson-Golabi-Behmel Syndrome via GPC3 Gene	ZW194	9981	Prevention Genetics Lab
Sotos Syndrome via the NSD1 Gene	ZW194	11529	Prevention Genetics Lab
Complete PKDx Evaluation	ZW127	8100	Athena Diagnostics

HNF1B Sequence Analysis	ZW221	21961	Baylor Medical Genetics Laboratories
Nephrolithiasis and Nephrocalcinosis Panel	ZW168	TH01	GeneDx, Inc.
Autosomal Dominant and Recessive Polycystic Kidney Disease (ADPKD and ARPKD) Panel	ZW194	10189	Prevention Genetics Lab
Congenital Abnormalities of the Kidney and Urinary Tract (CAKUT) Panel	ZW194	2667	Prevention Genetics Lab
Focal Segmental Glomerulosclerosis (FSGS) via the ANLN Gene	ZW194	91602	Prevention Genetics Lab
Hereditary Cystic Kidney Diseases Panel	ZW194	10619	Prevention Genetics Lab
Nephrotic Syndrome (NS)/Focal Segmental Glomerulosclerosis (FSGS) Panel	ZW194	10417	Prevention Genetics Lab
NPHP1 Deletion Test (Familial Juvenile Nephronophthisis)	ZW127	750	Athena Diagnostics
Alport Syndrome NGS Panel Comprehensive	ZW193	5144	Connective Tissue Gene Tests Lab
JAG1 Sequence Analysis	ZW221	3755	Baylor medical Genetics Laboratories
LMX1B Comprehensive - Sequence and Deletion/Duplication Analysis	ZW221	7523	Baylor medical Genetics Laboratories
OCRL Gene Sequencing	ZW168	TA73	GeneDx, Inc.
Alport Syndrome (AS) Panel	ZW194	10147	Prevention Genetics Lab
Autosomal Dominant and Recessive Polycystic Kidney Disease (ADPKD and ARPKD) Panel	ZW194	10189	Prevention Genetics Lab
Bartter Syndrome Type 1 via the SLC12A1 Gene	ZW194	11669	Prevention Genetics Lab
Dent Disease Panel	ZW194	10077	Prevention Genetics Lab
Distal Renal Tubular Acidosis Panel	ZW194	10159	Prevention Genetics Lab
Nephronophthisis and Joubert Syndrome via the NPHP1 Gene	ZW194	15261	Prevention Genetics Lab
Nephronophthisis and Senior-Loken Syndrome Sequencing Panel	ZW194	10341	Prevention Genetics Lab
Renal Hypomagnesemia 3 via the CLDN16 Gene	ZW194	8921	Prevention Genetics Lab

Questions

Contact Michelle Raths, Laboratory Technologist Resource Coordinator at 800-533-1710.